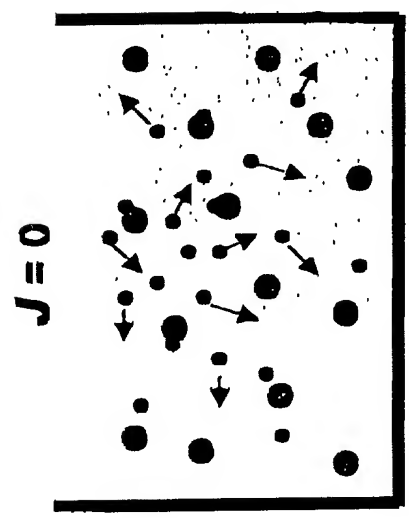
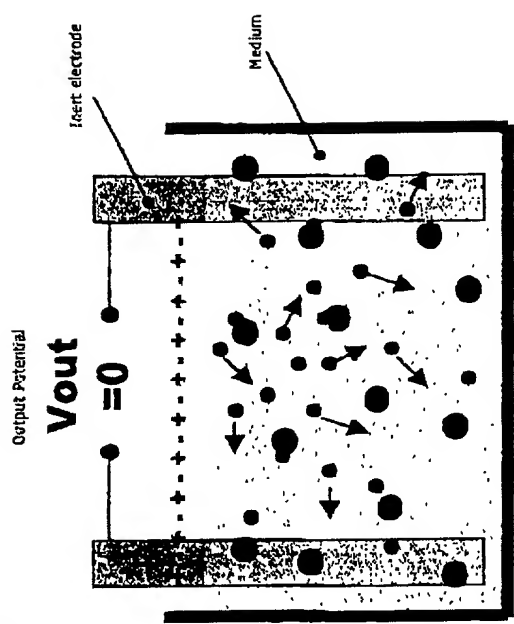


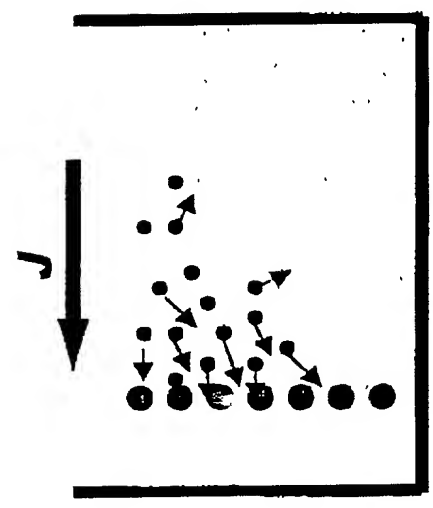
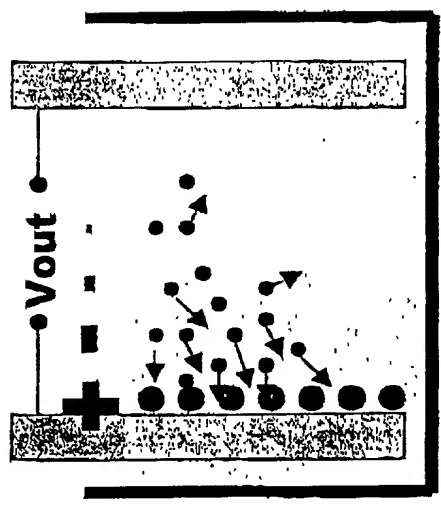
$A \rightleftharpoons B$
 $\bullet + \bullet \rightarrow \bullet$

J : Current Density of B



1.1

1.1) If A and B are both free in the medium no net transient gradient of molecules (current density) is created.



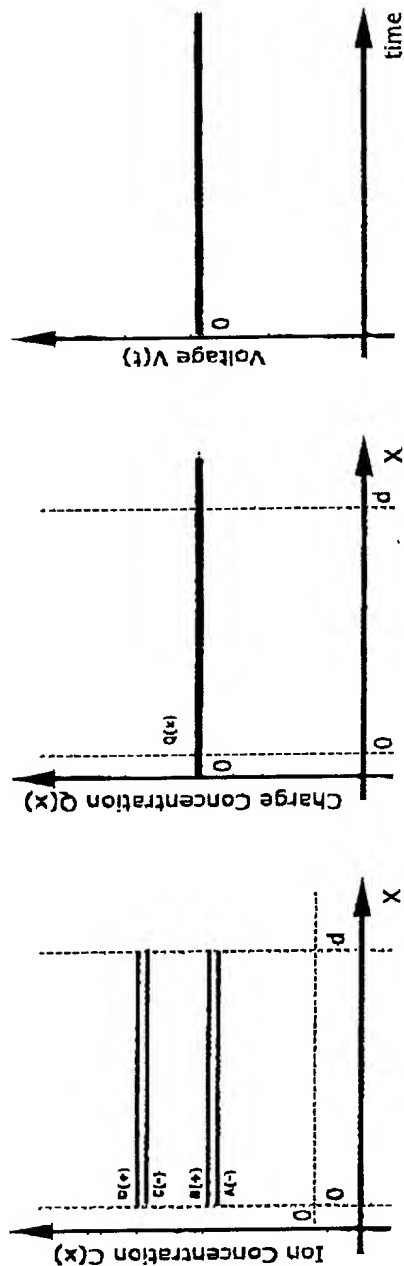
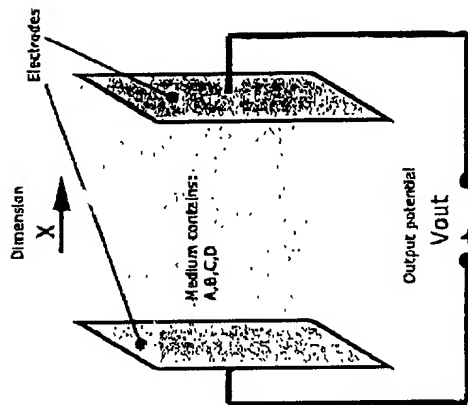
1.2

1.2) If A is spatially immobilized and B is free in the medium, the reaction causes a net transient gradient (current density) of B toward A. This transient current creates a temporary potential difference in the medium.

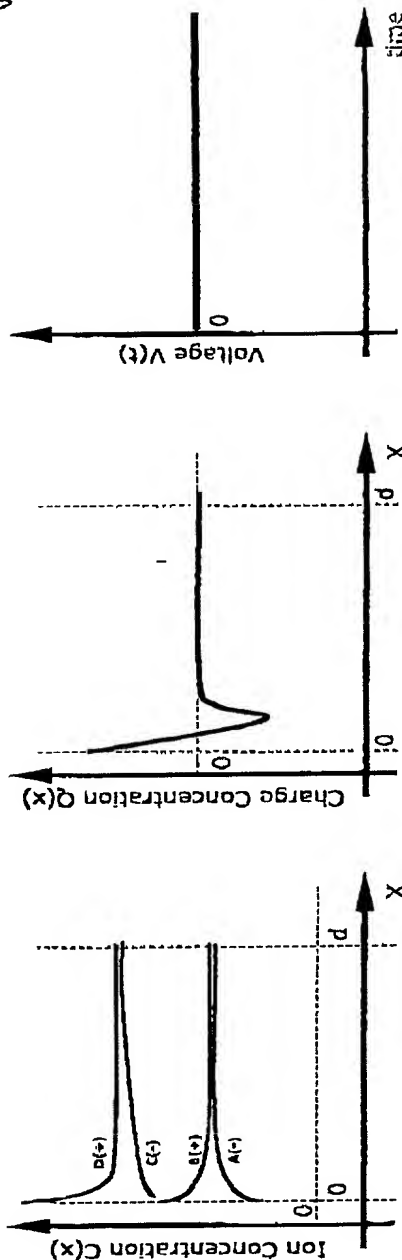
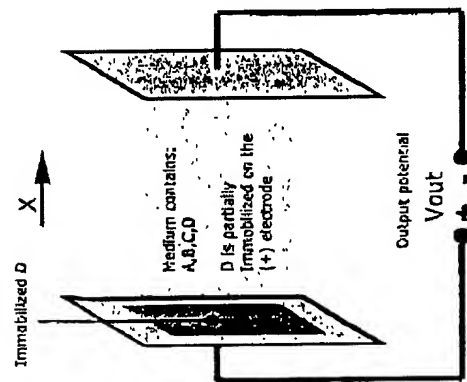
1/35

1.3 Potential difference between electrodes equilibrium (steady state):

- 1) Electrodes are inert and do not interact with medium.
- 2) Four molecules (ions) A, B, C and D are present in the medium.
- 3) Molecules have arbitrary diffusion length and charge.



1.3.a) All molecules are free in the medium. Concentration of all molecules is uniform in equilibrium.

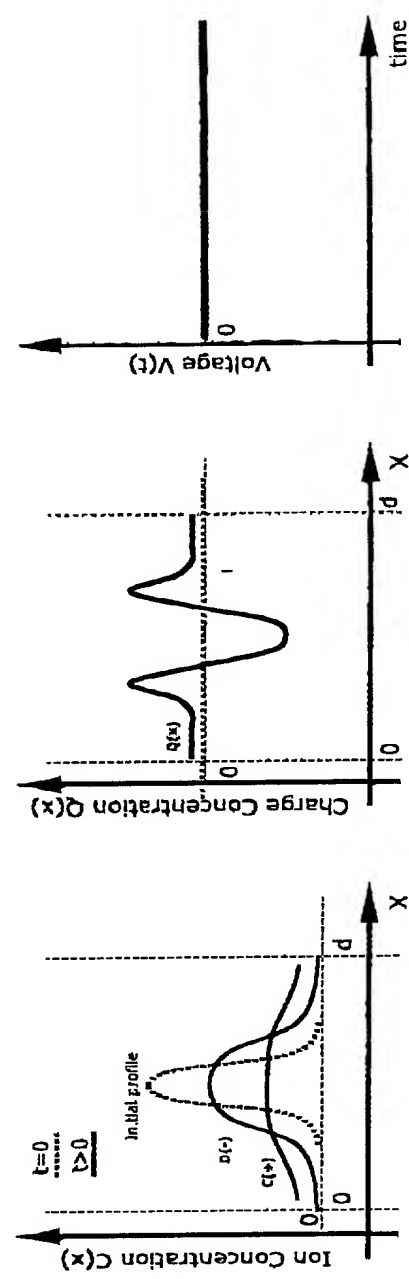
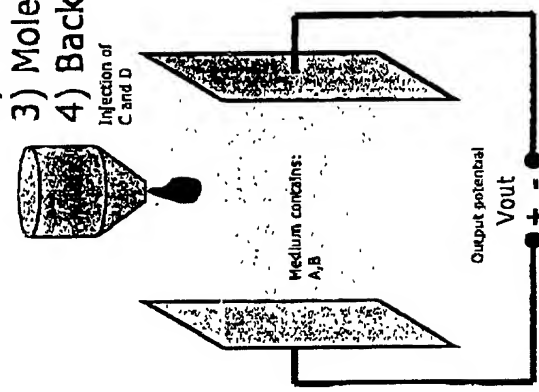


1.3.b) D is partially immobilized on the surface of the (+) Electrode which forces a none uniform concentration of molecules.

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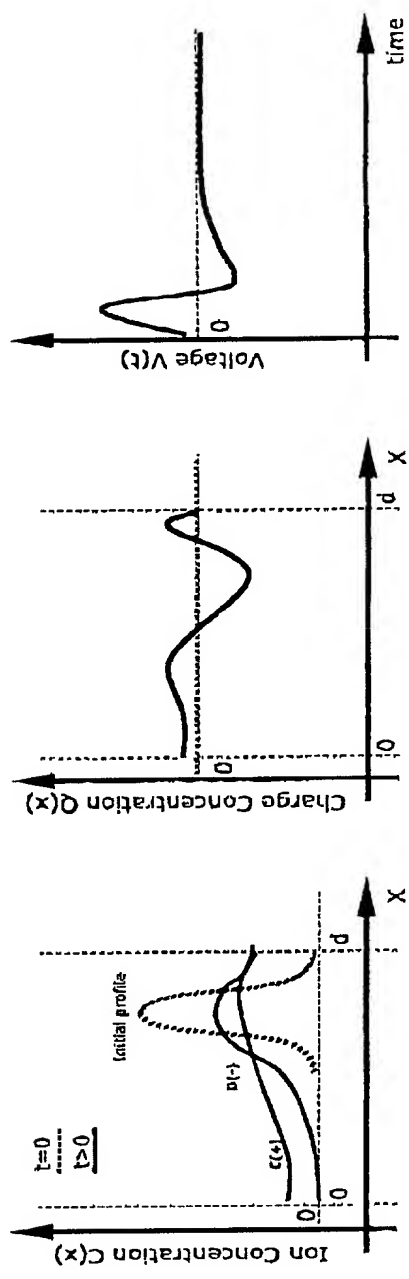
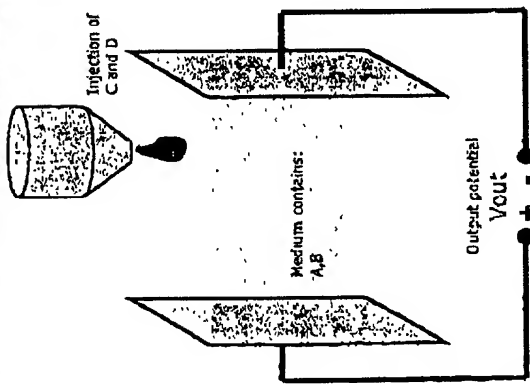
1.4 Potential difference between electrodes in none-equilibrium (transient) state:

- 1) Electrodes are inert and do not interact with the medium.
- 2) Two molecules (ions) are present in the medium and two are added.
- 3) Molecules have arbitrary diffusion length and charge.
- 4) Background molecules are not shown (A and B).



1.4.a) C and D are added symmetric to the electrodes.

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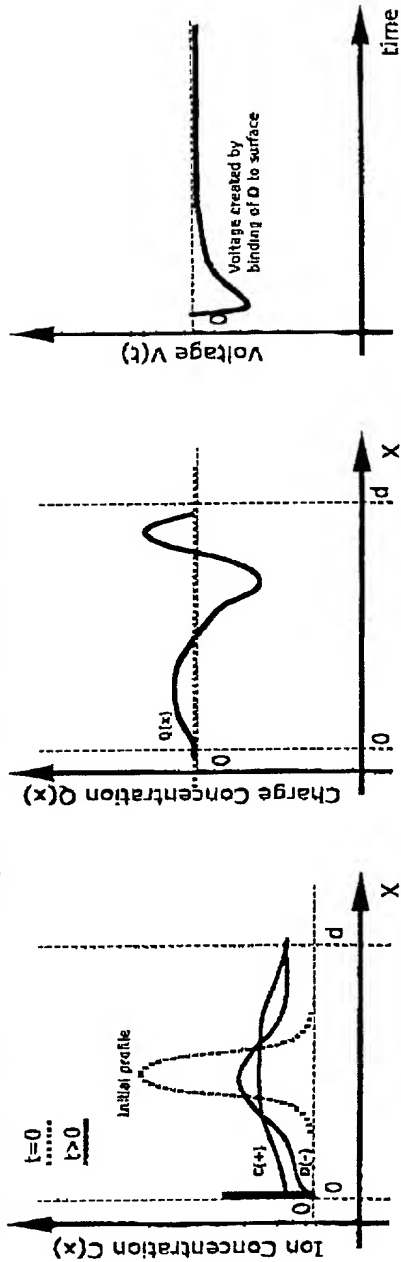
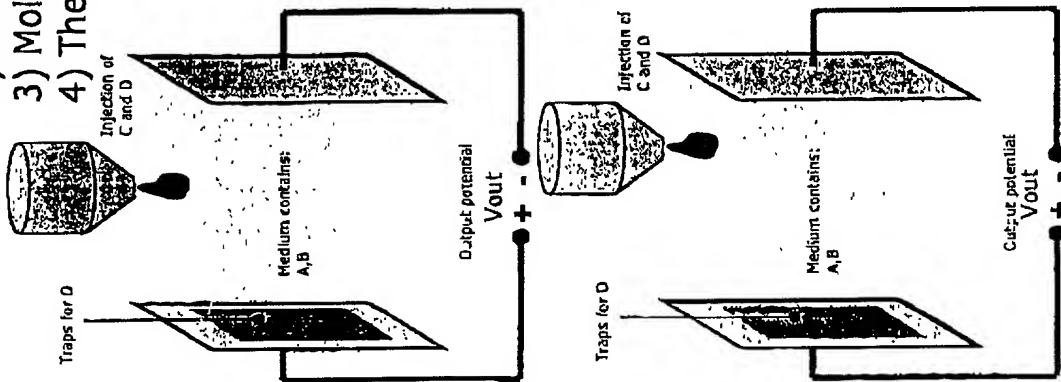


1.4.b) C and D are added asymmetric to the electrodes and an ionic perturbation is generated.

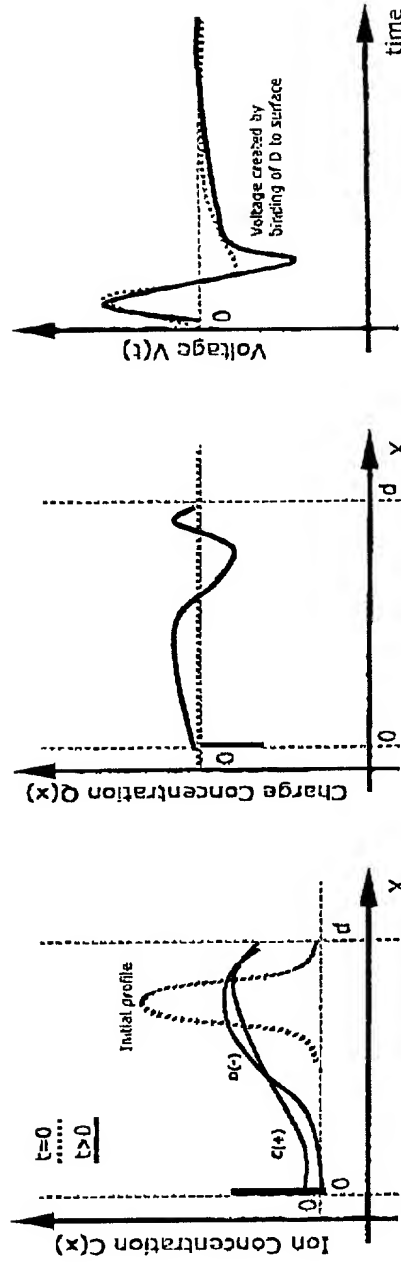
1.5

Potential difference between electrodes in the none-equilibrium (transient) with surface trap:

- 1) Electrodes are inert and do not interact with the medium.
- 2) two molecules (ions) are present in the medium and two are added in time.
- 3) Molecules have arbitrary diffusion length and charge.
- 4) The (+) electrode has finite traps for D on the surface.



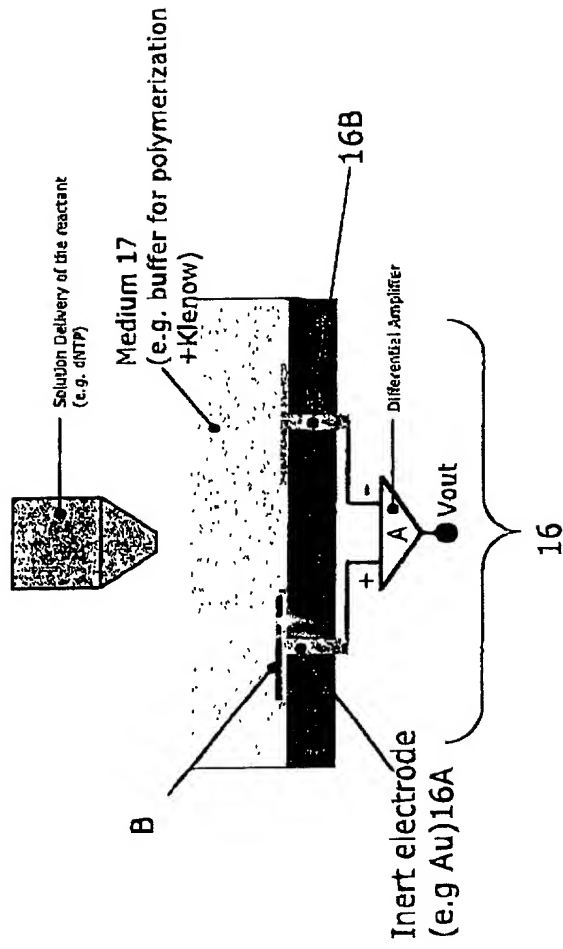
1.5.a) C and D are added symmetric to the electrodes. Traps cause a potential perturbation.



1.5.b) C and D are added asymmetric to the electrodes, and an extra electric field perturbation is created by the traps.

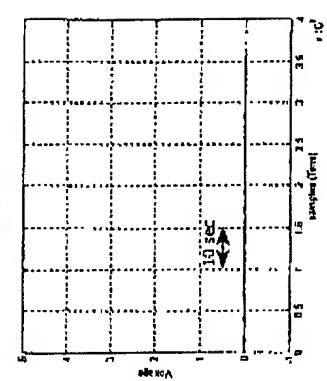
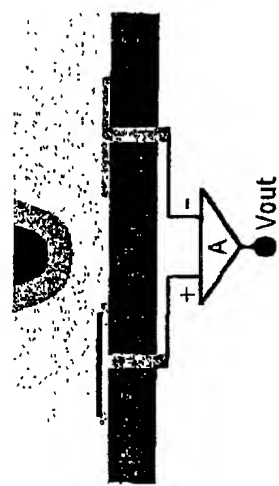
2.1 Planar sensor design example:

- 1) Electrodes are inert and do not interact with the medium.
- 2) The target molecules are immobilized on the (+) electrode.
- 3) The (-) electrode is the reference electrode.
- 4) A differential amplifier subtracts the voltage from the two electrodes.

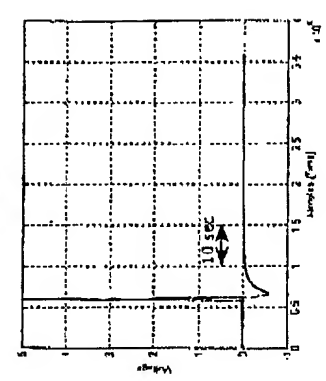
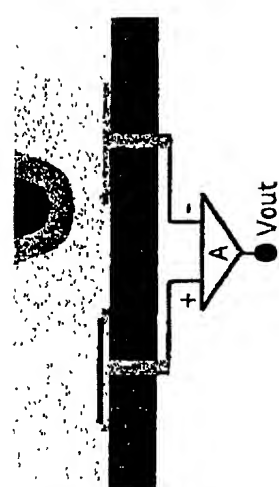
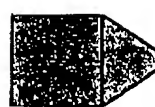


2.2 Example of signal generated when no binding at the surface occurs :

- 1) Electrodes are inert and do not interact with the medium.
- 2) The target molecules are immobilized on the (+) electrode.
- 3) The (-) electrode is the reference electrode.
- 4) A differential amplifier subtracts the voltage of the two electrodes.



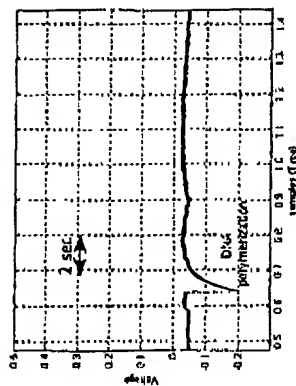
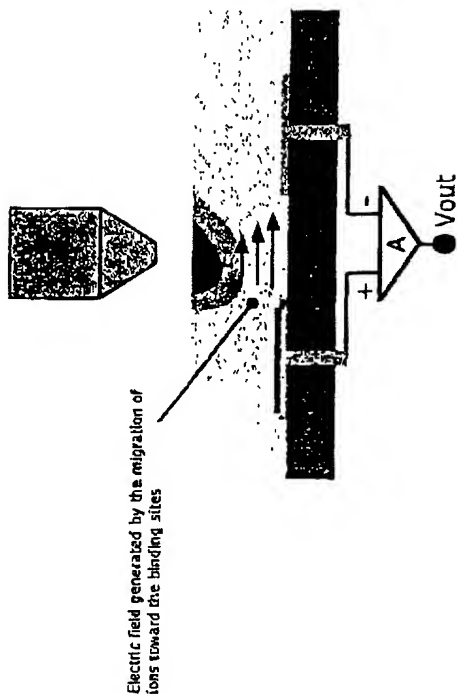
a) Solution is delivered symmetric to the electrodes
With 0.1 pmol immobilized ssDNA.



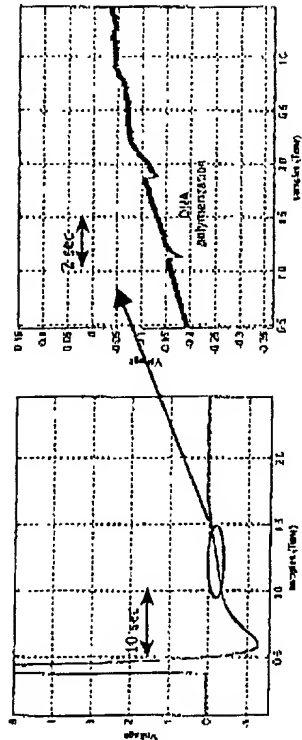
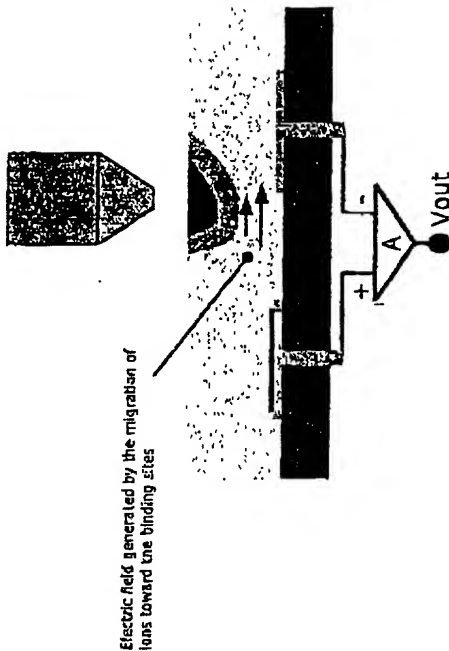
b) Solution is delivered asymmetric to the electrodes
With 0.1 pmol immobilized ssDNA.

2.3 Example of signal generated when binding at the surface occurs:

- 1) Electrodes are inert and do not interact with the medium.
- 2) The target molecules are immobilized on the (+) electrode.
- 3) The (-) electrode is the reference electrode.
- 4) A differential amplifier subtracts the voltage from the two electrodes.

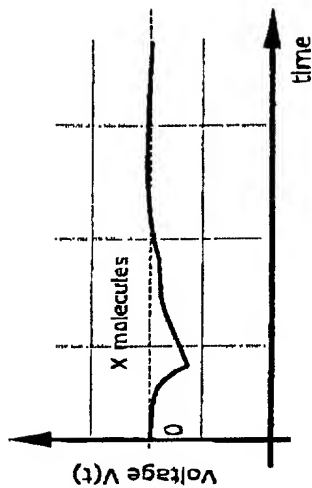
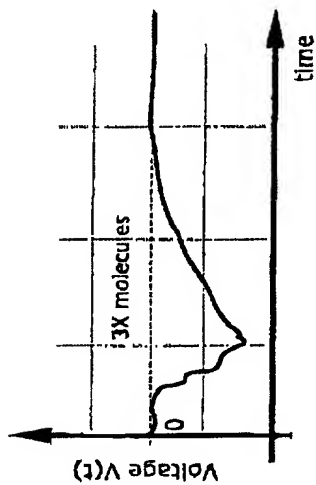


a) Solution is delivered symmetric to the electrodes, Polymerization of 0.1 pmol primed ssDNA.

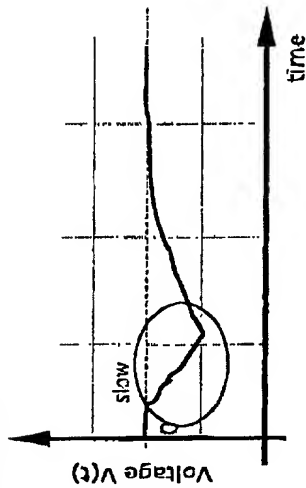
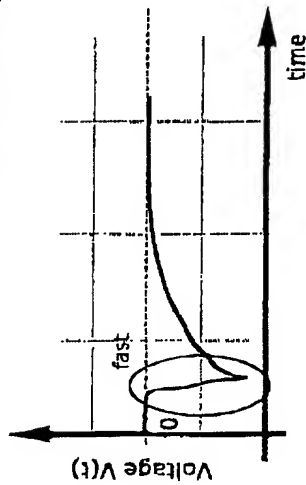


b) Solution is delivered asymmetric to the electrodes, Polymerization of 0.1 pmol primed ssDNA.

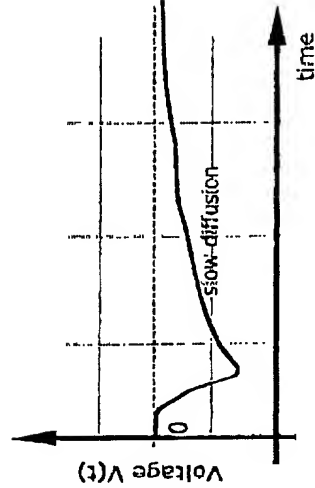
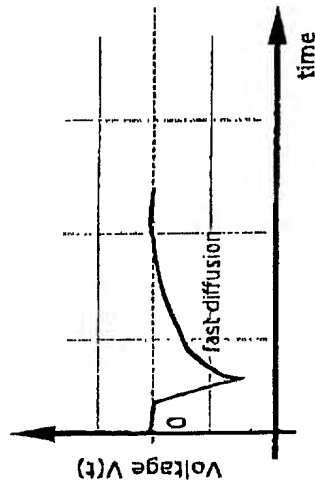
2.4 Analysis examples of the transient signal generated:



a) Quantity of molecules



b) Kinetics (speed) of the reaction



a) Movement and diffusion of molecules.

FIGURE 3:
Sequencing

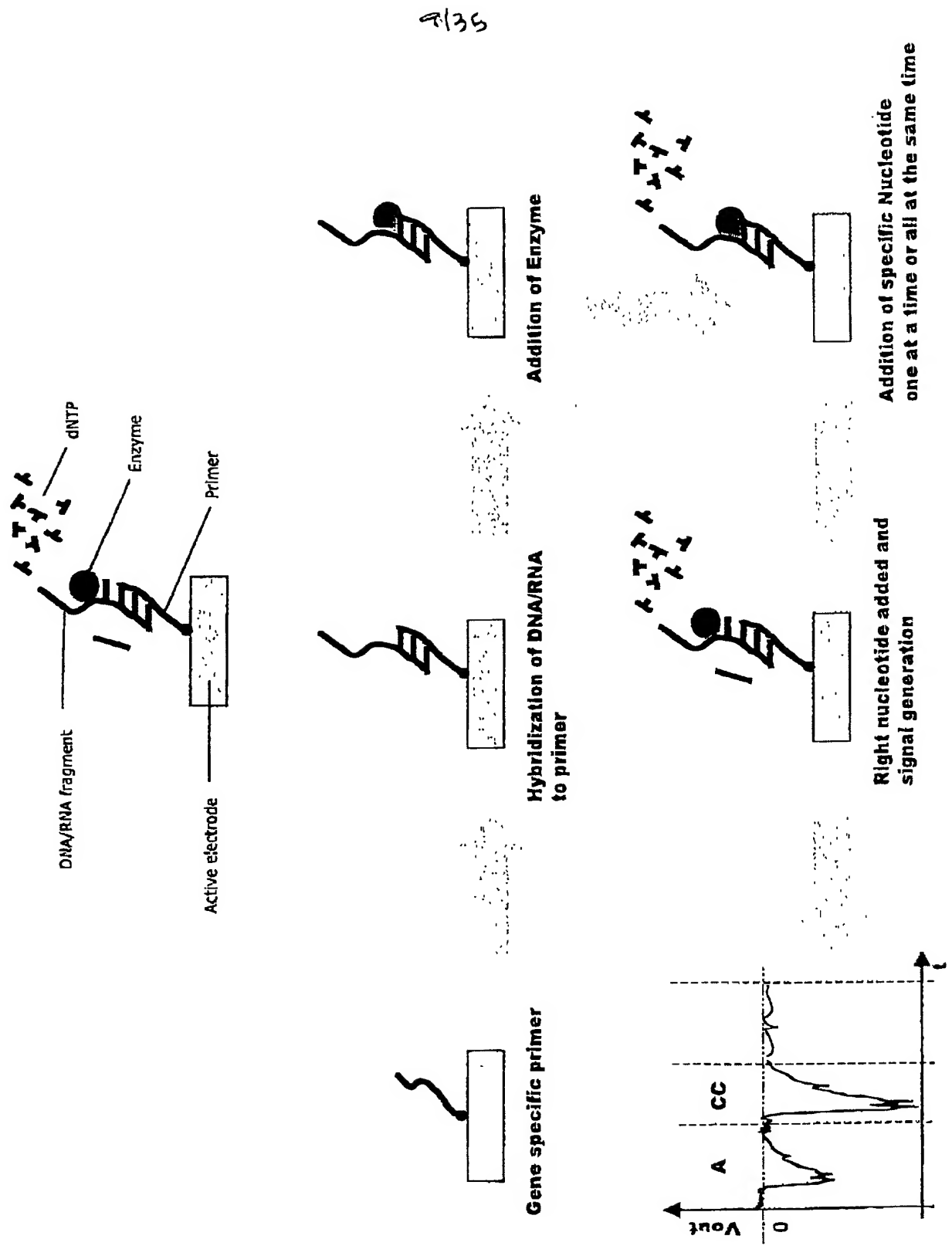
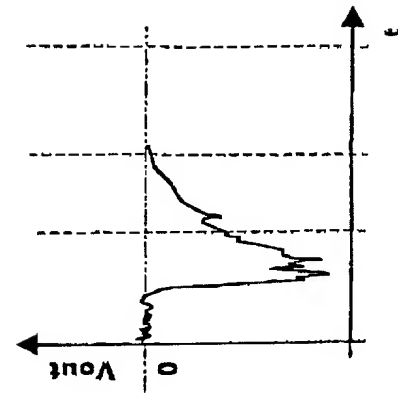
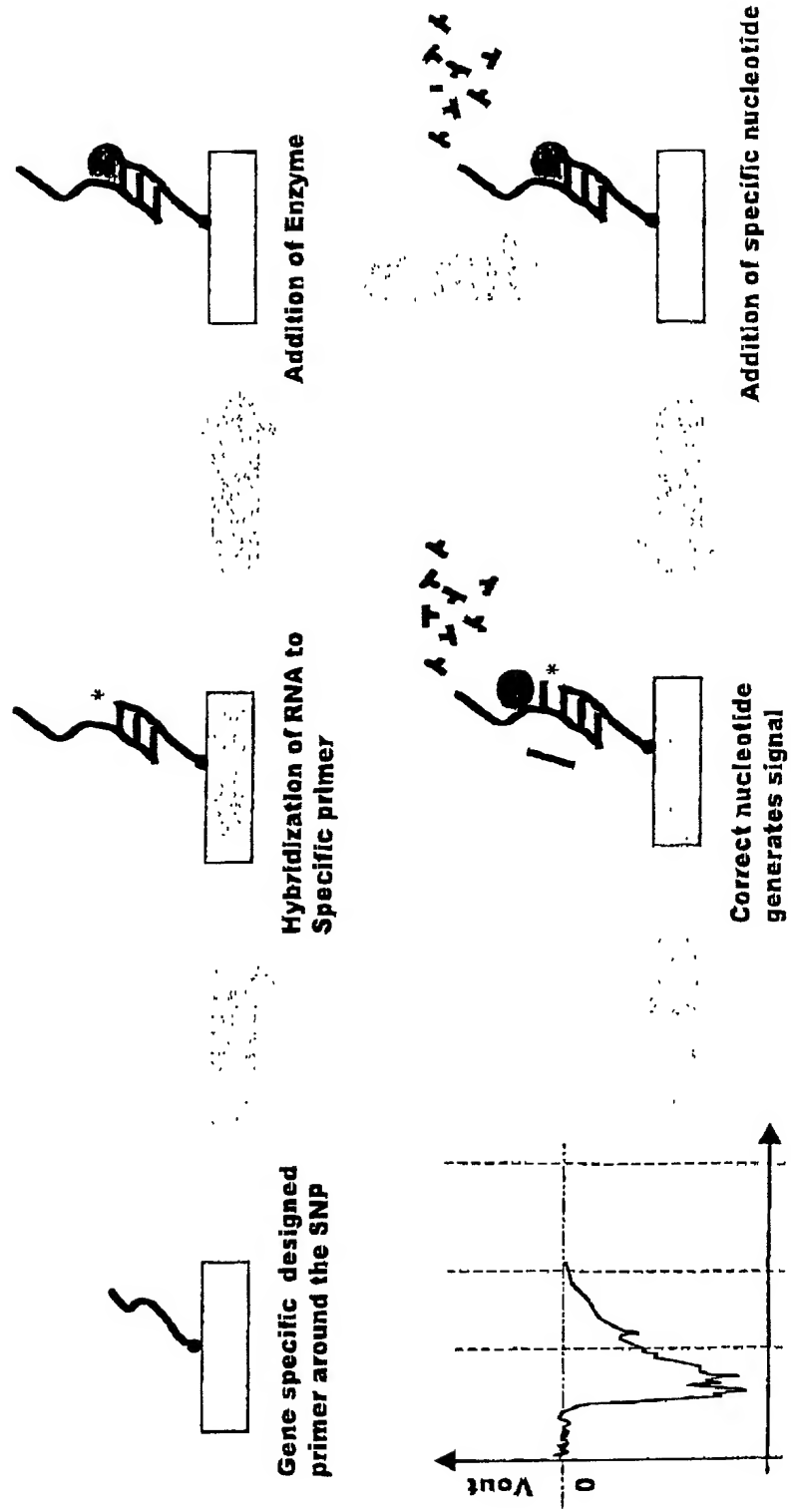
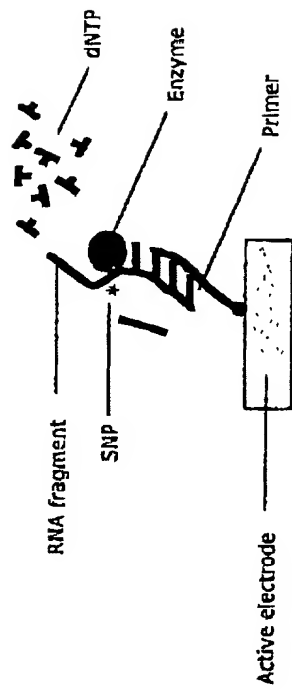
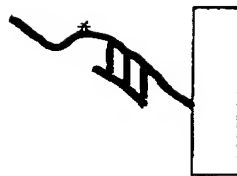
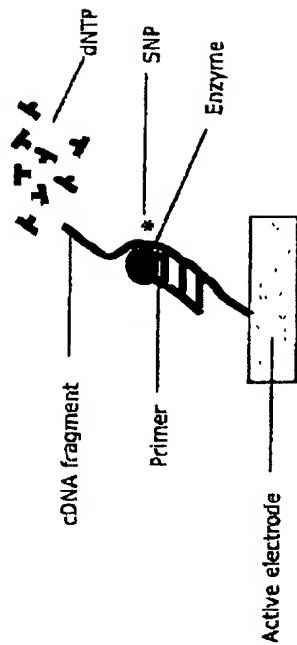


FIGURE 4:1
SNP detection by using Total RNA



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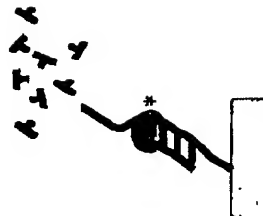
FIGURE 4:2
SNP detection by using cDNA



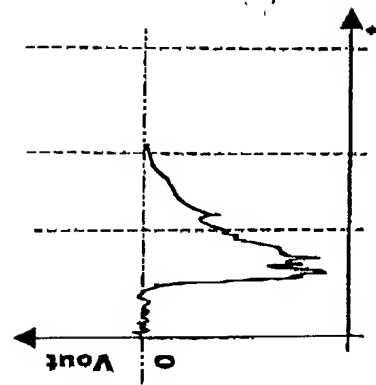
Annealing the specific designed primer around the SNP



Addition of Enzyme



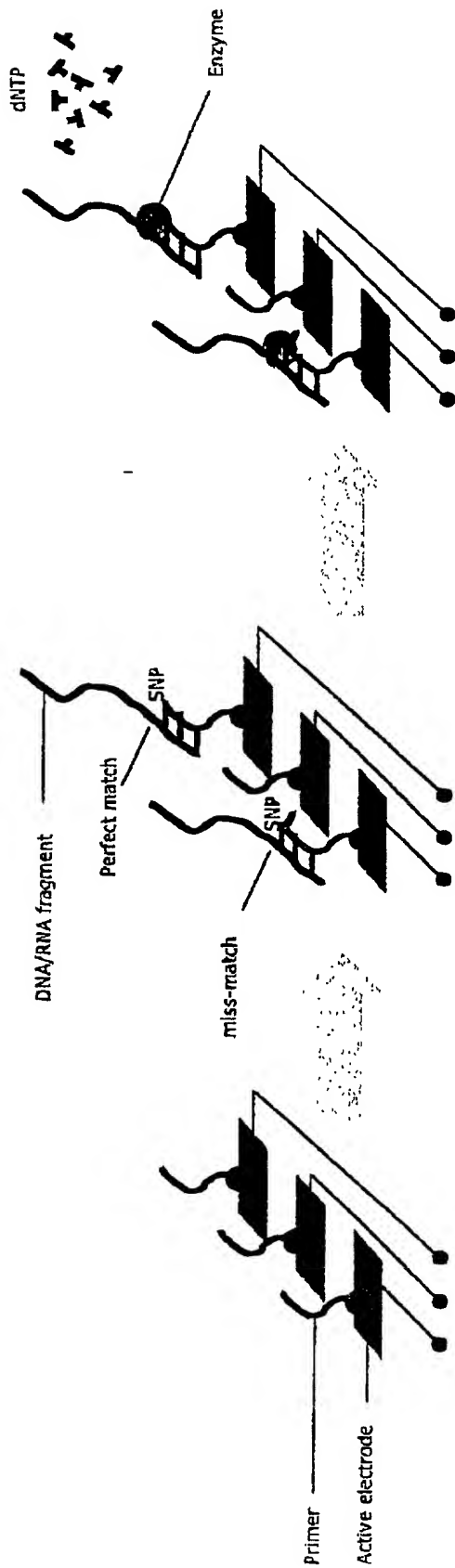
Addition of specific nucleotide



Right nucleotide added and signal generation

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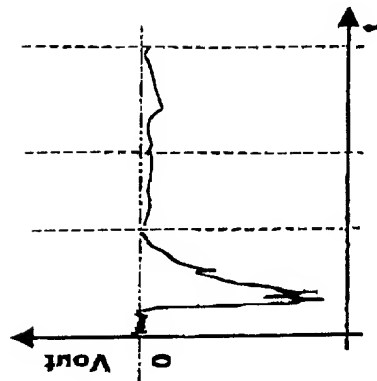
FIGURE 4:3
SNP detection by using
allele specific primer



Addition of Enzyme & dNTP

Hybridization of DNA/RNA to primer

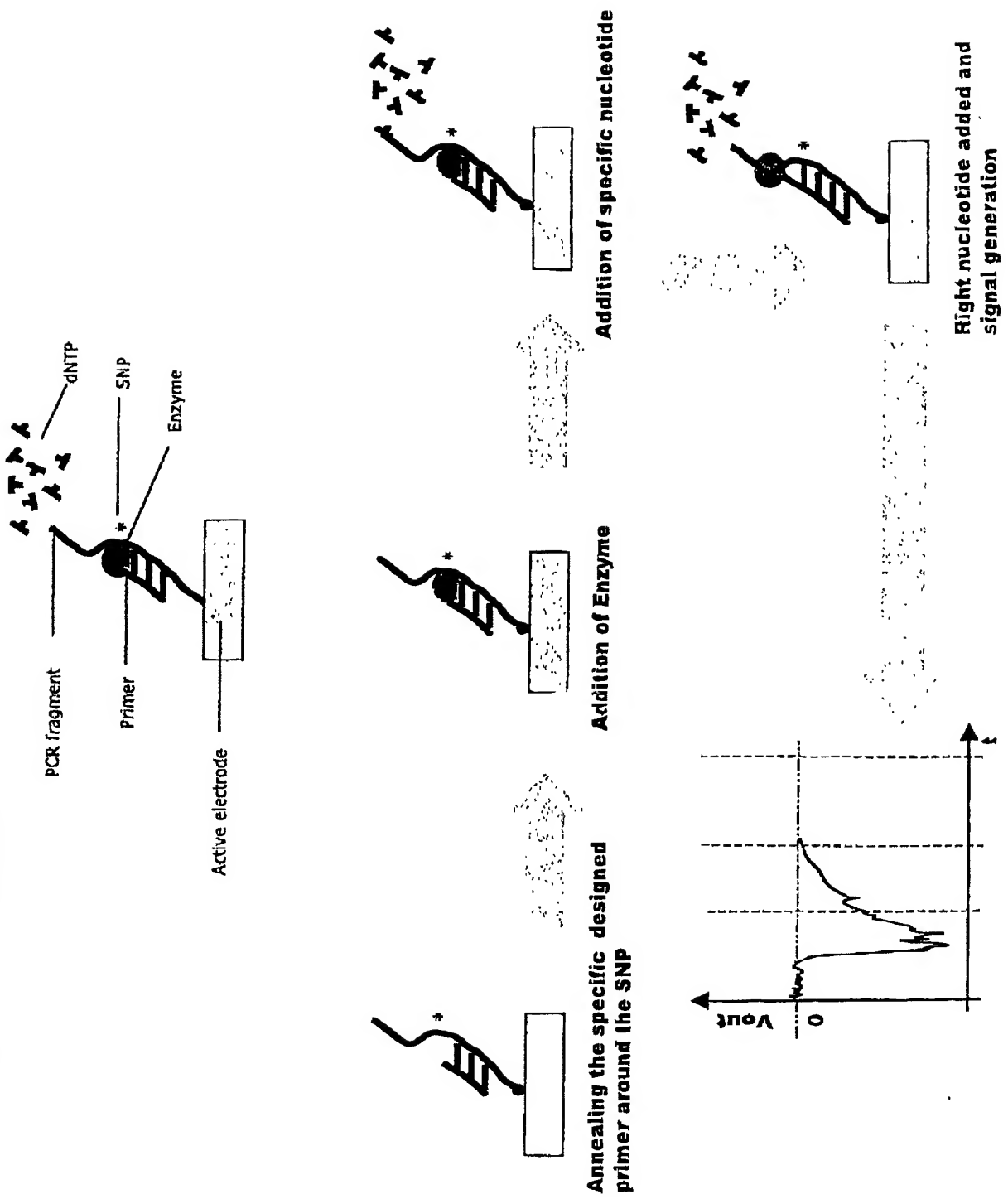
Allele specific primers



Perfect match primer/template polymerizes and signal is generated

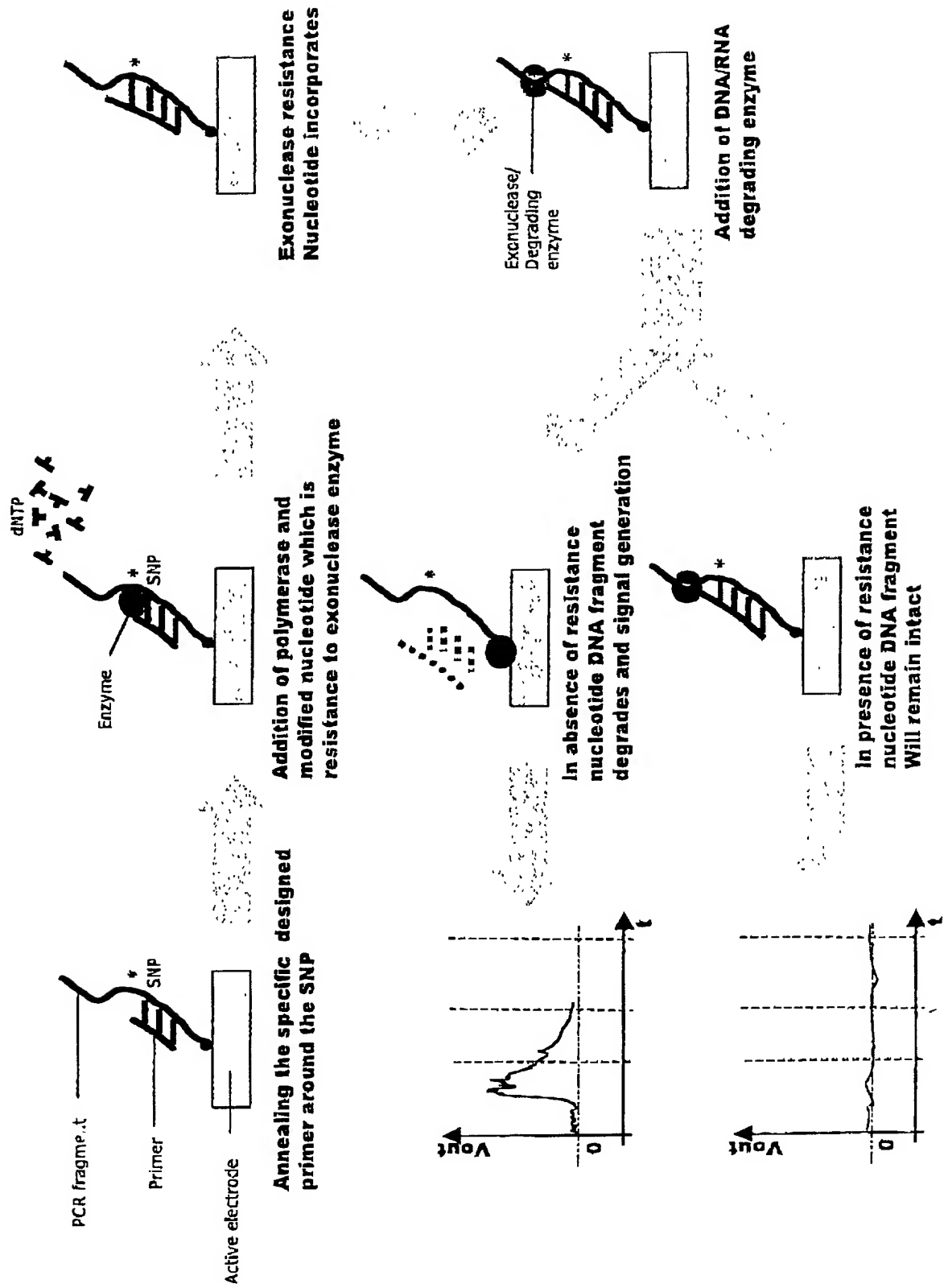
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FIGURE 5:
SNP detection by using PCR product



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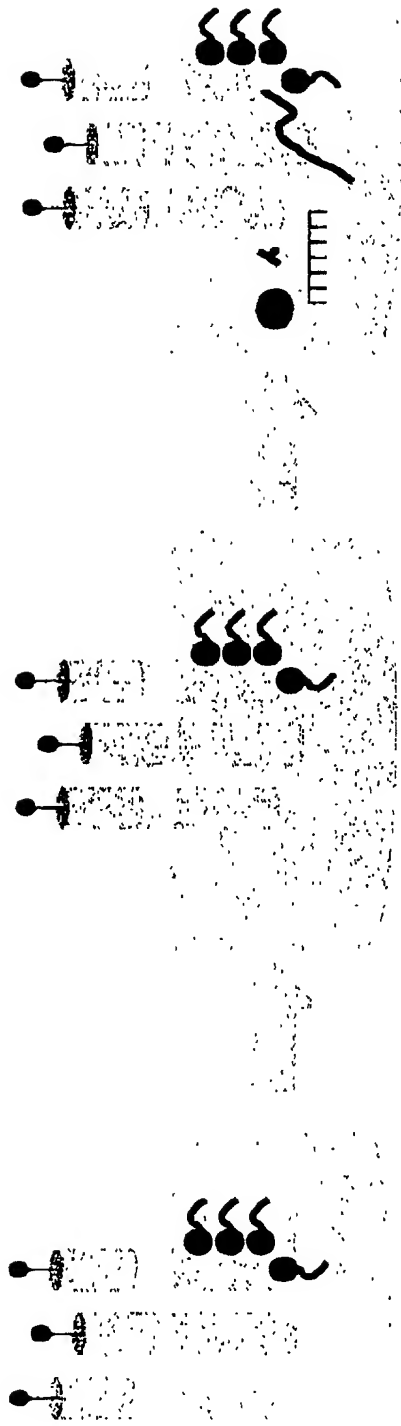
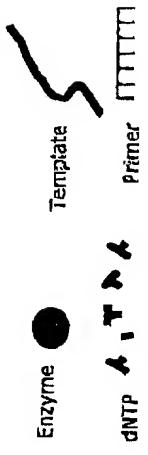
FIGURE 6:
SNP detection by using Exonuclease/
Degrading enzyme



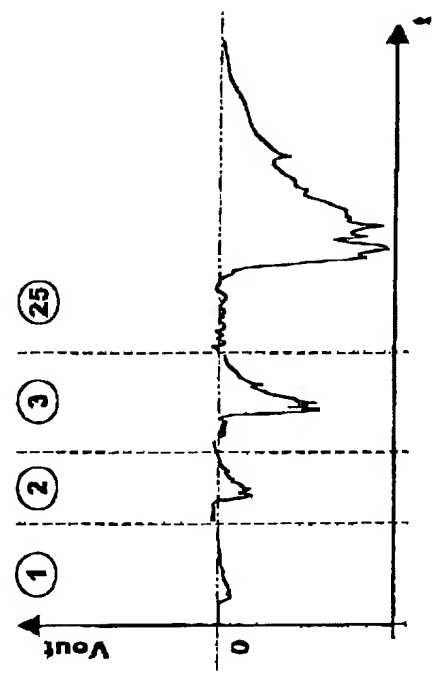
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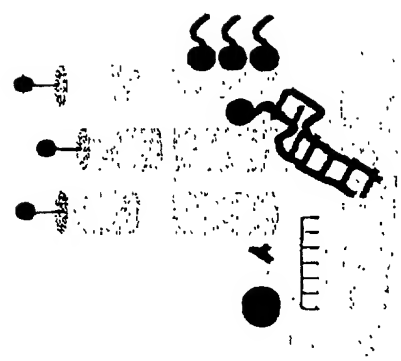
**FIGURE 7:
Real time PCR**



Addition of dNTP, enzyme
and secondary primer

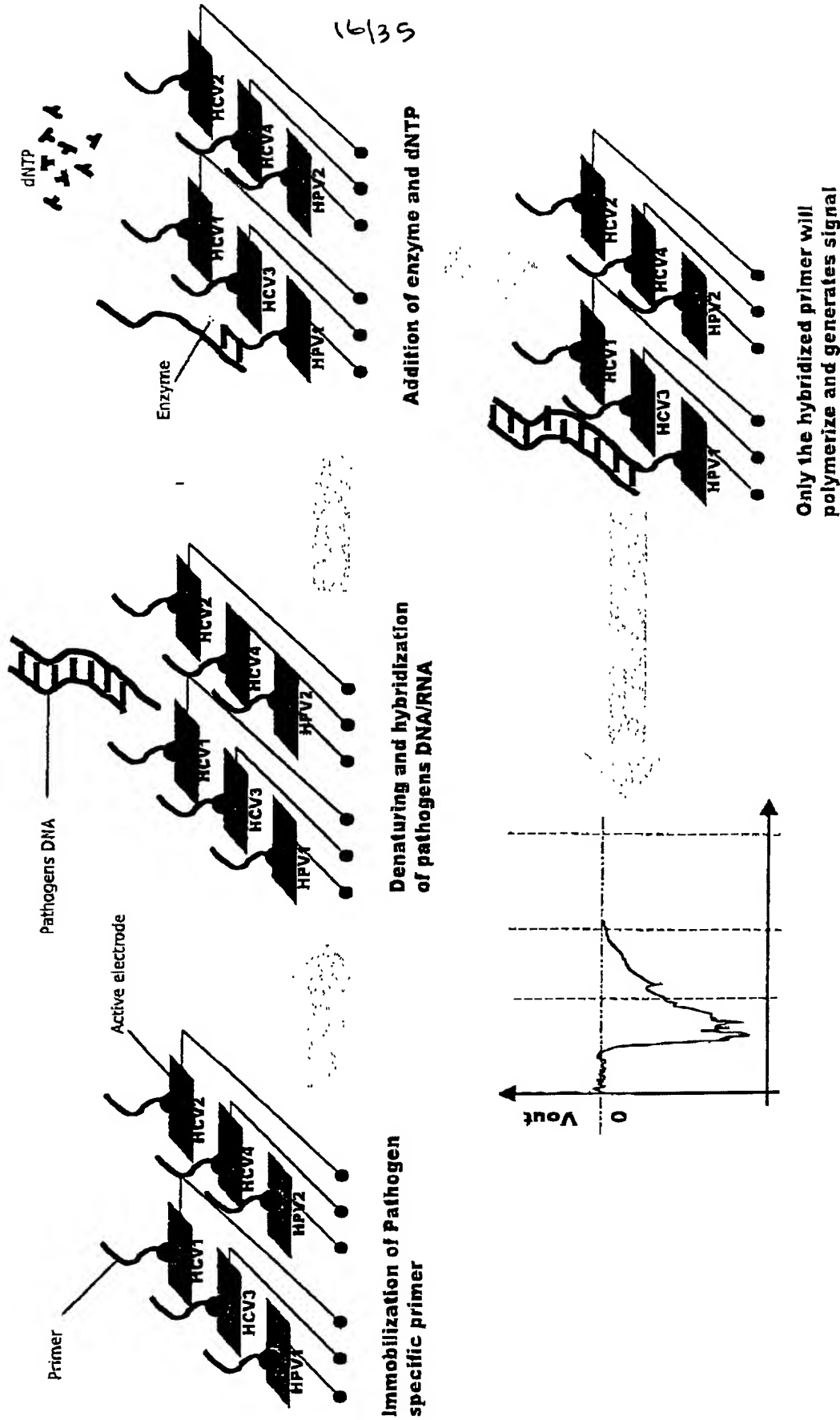


PCR mixture are ready for
amplification



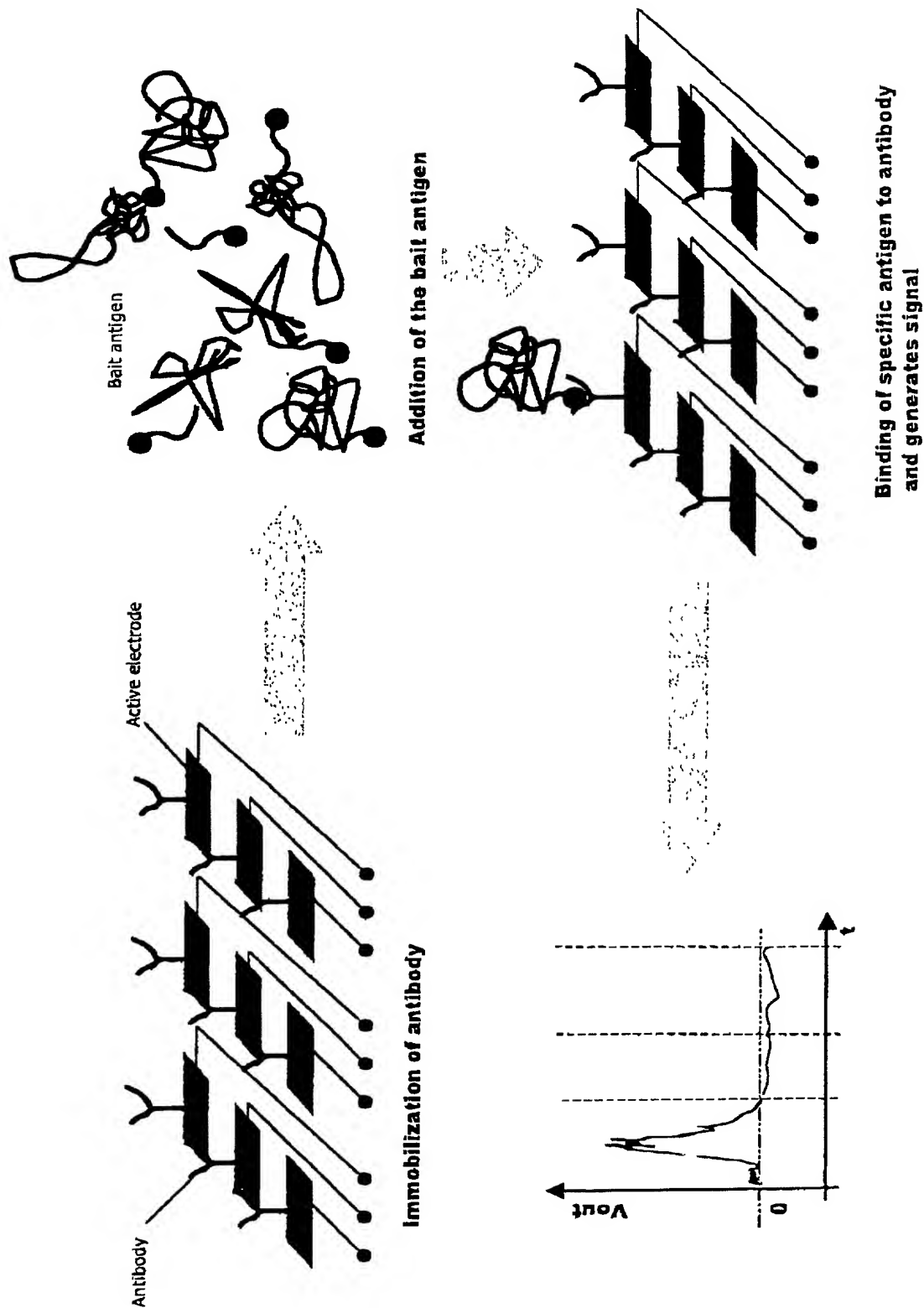
Signal generation due to
polymerization in each cycle

FIGURE 8:
Pathogen typing



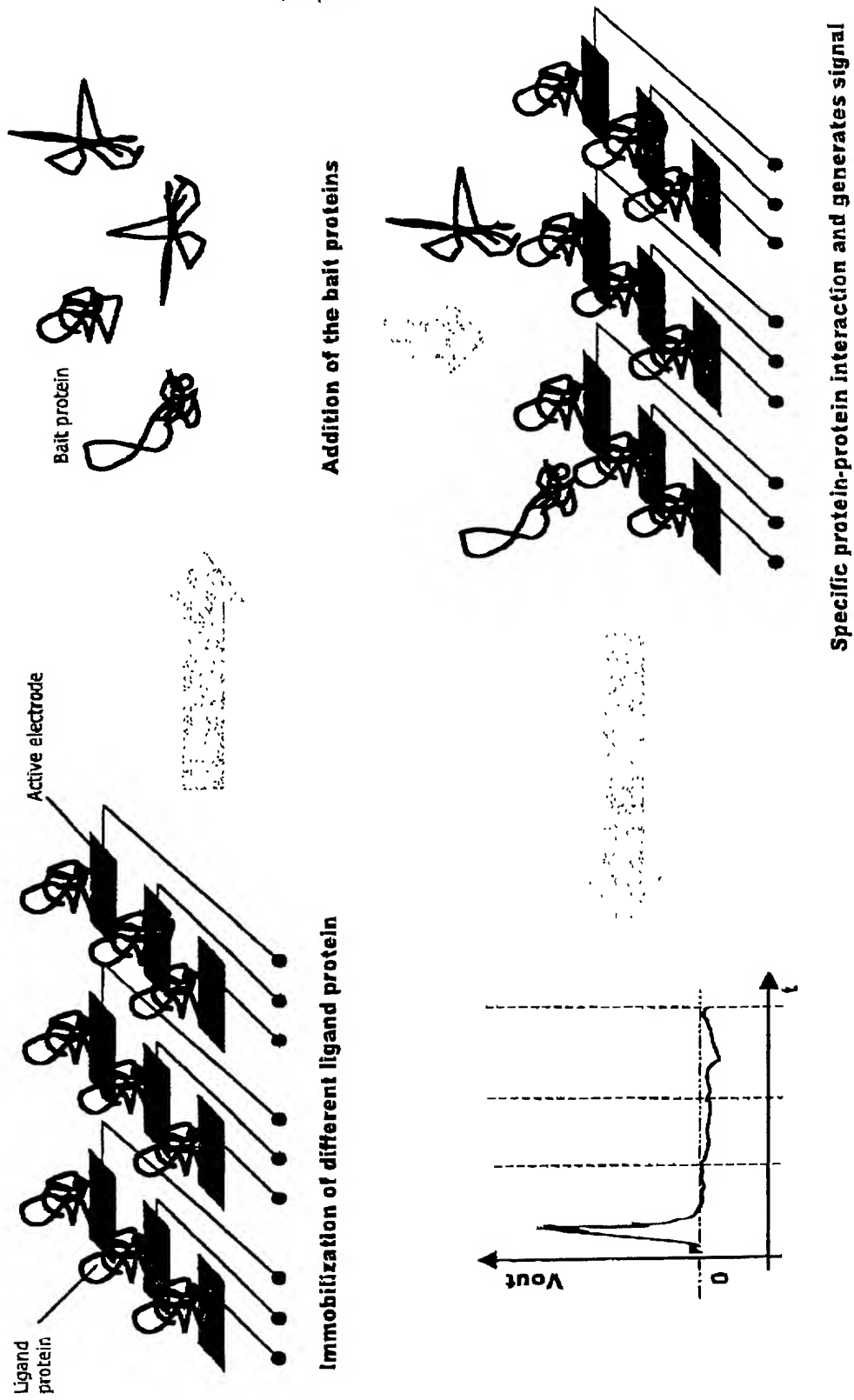
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FIGURE 9:
Antigen-antibody detection



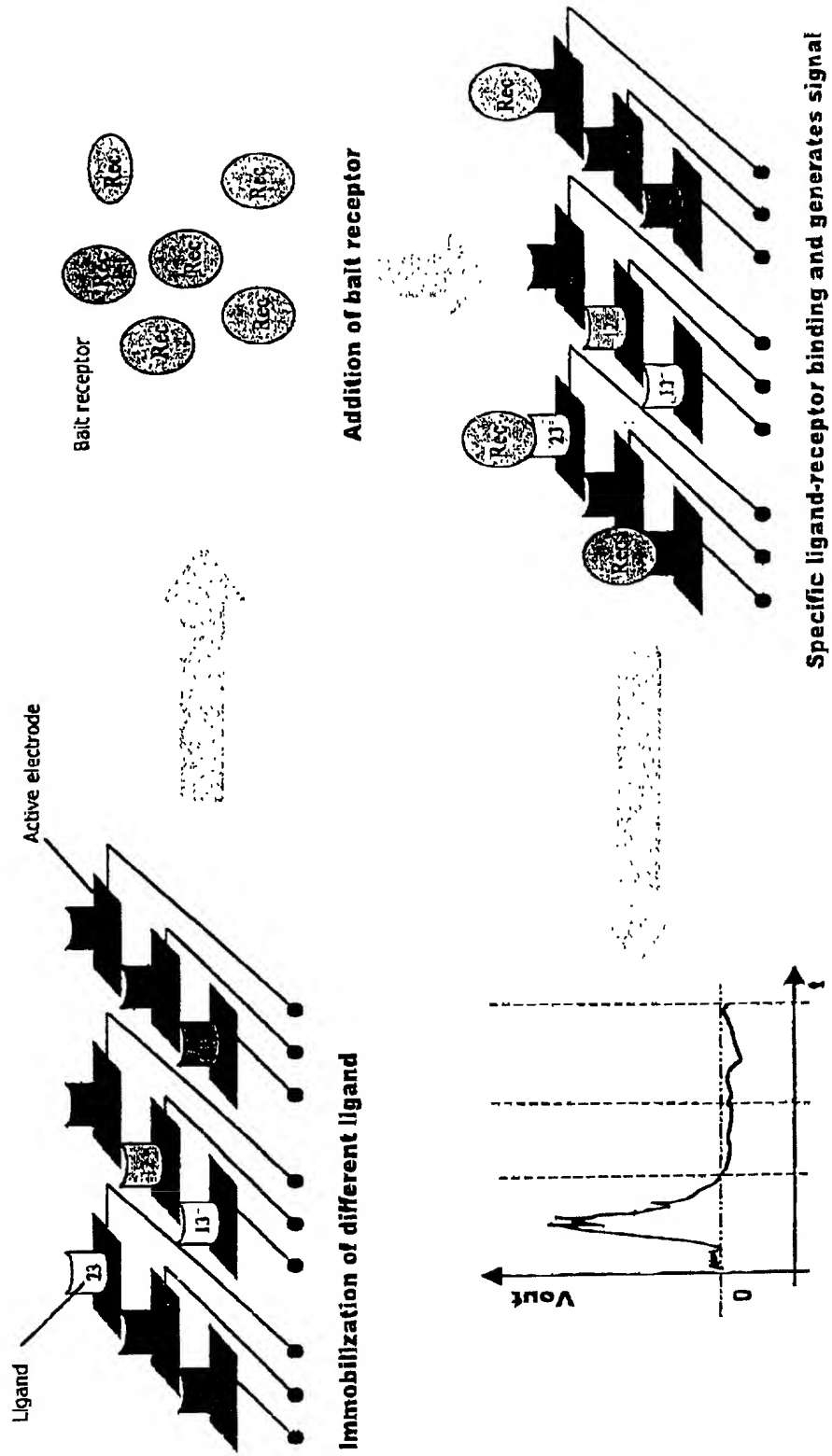
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FIGURE 10:
Protein-protein interaction



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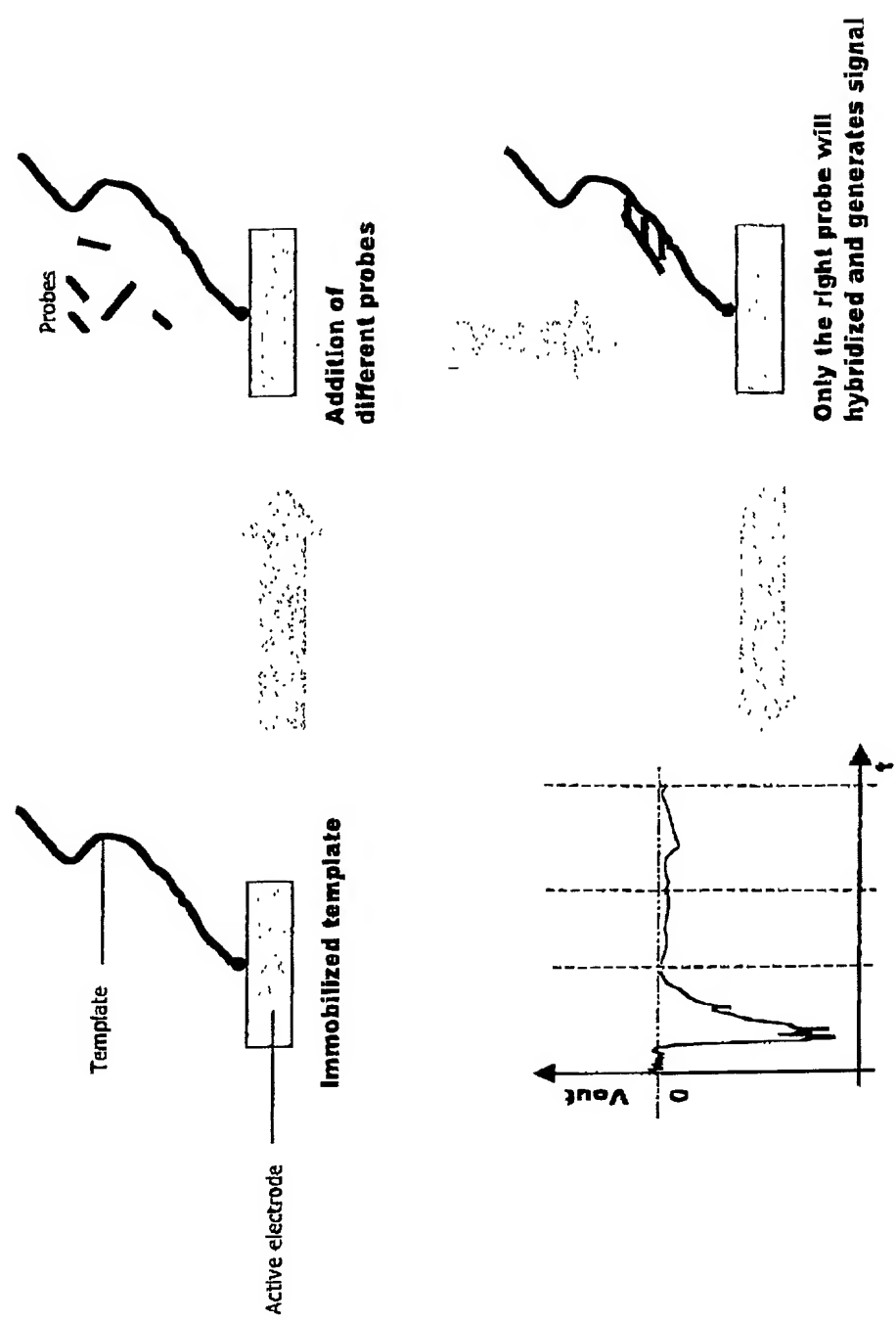
FIGURE 11:
Ligand and receptor detection



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FIGURE 12:
Hybridization



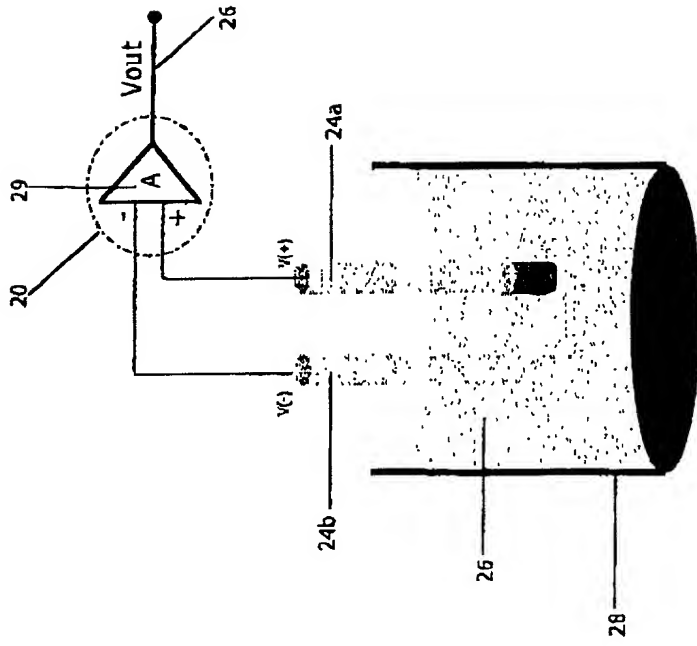


Fig: 13

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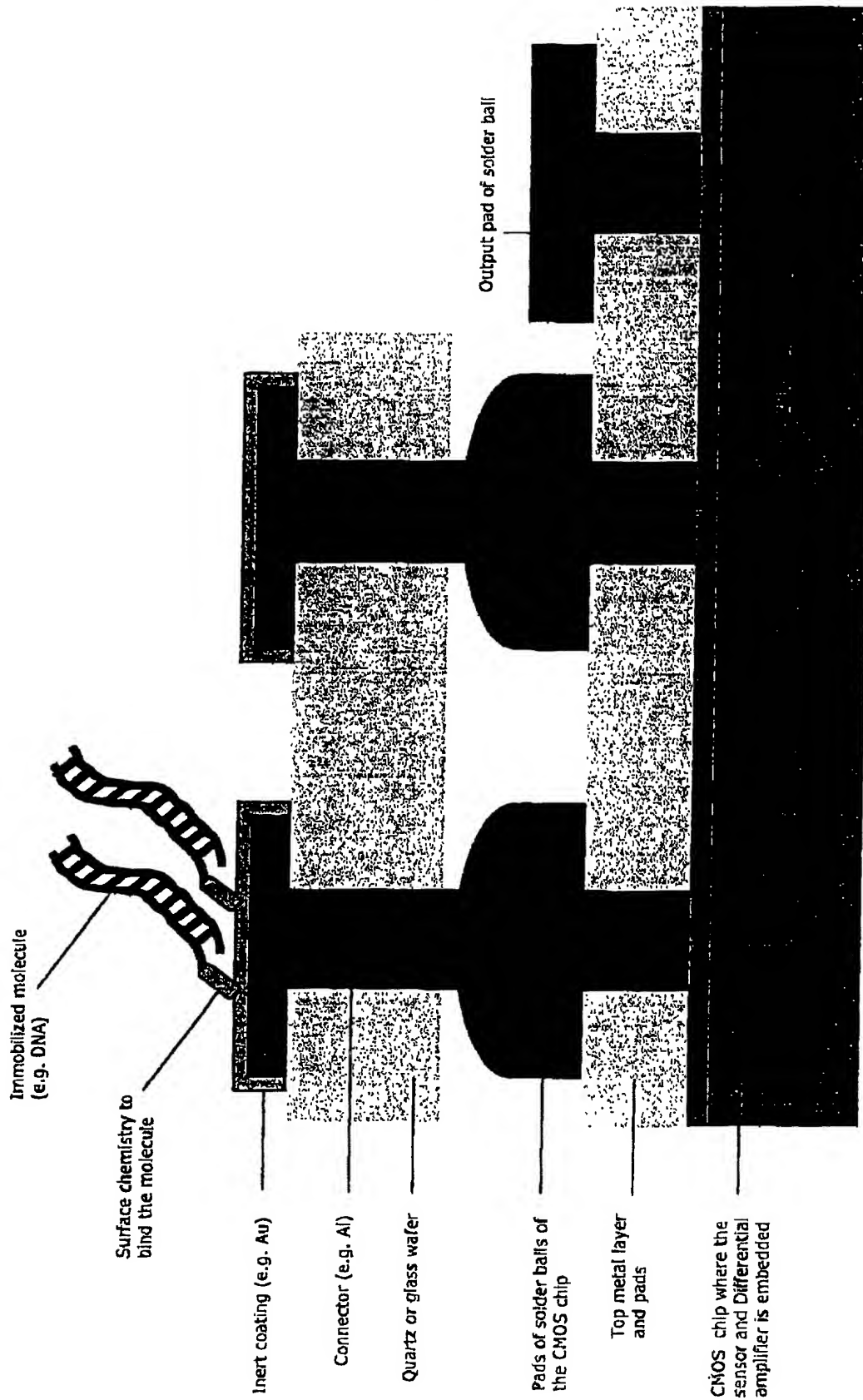


Fig: 14

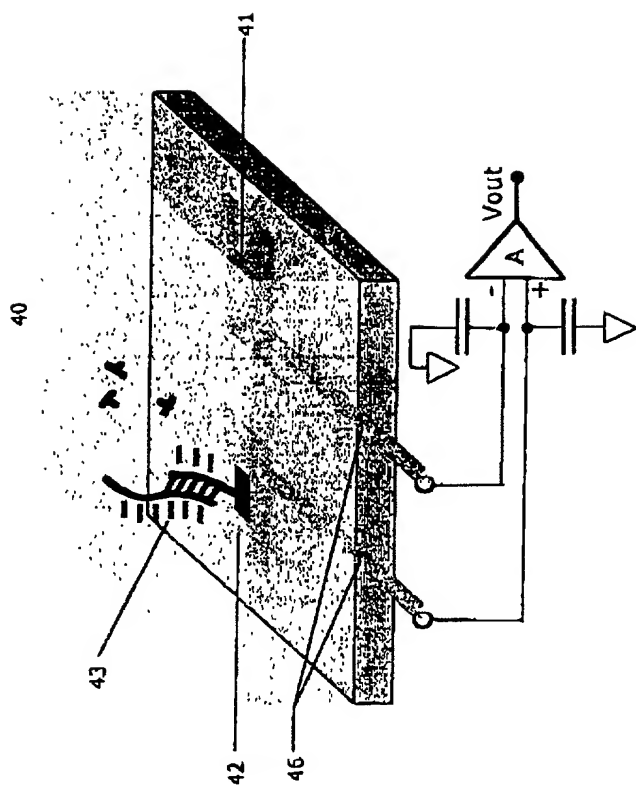


Fig: 15

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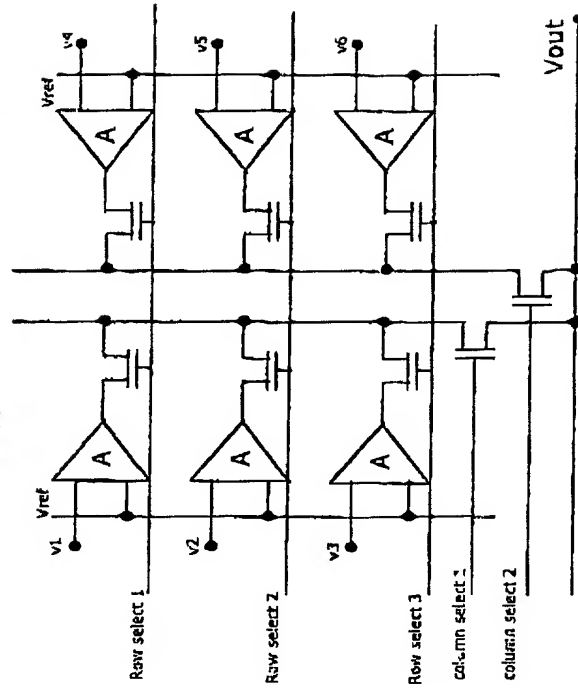
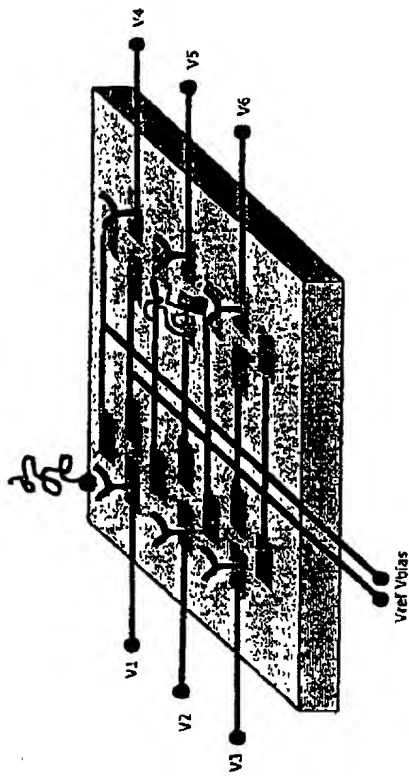
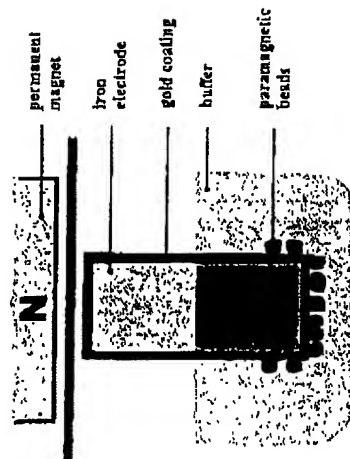


Fig: 16

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Figure 17A: PCR product attracts to an electrode by using a permanent magnet and paramagnetic beads.



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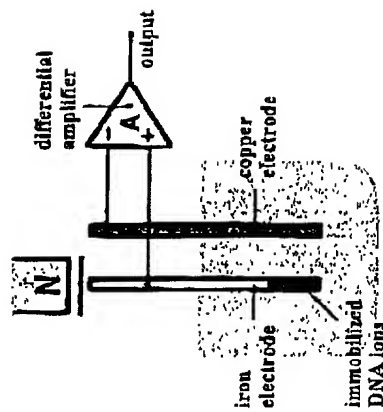


Figure 17 B: Basic model of the sensor with a differential amplifier

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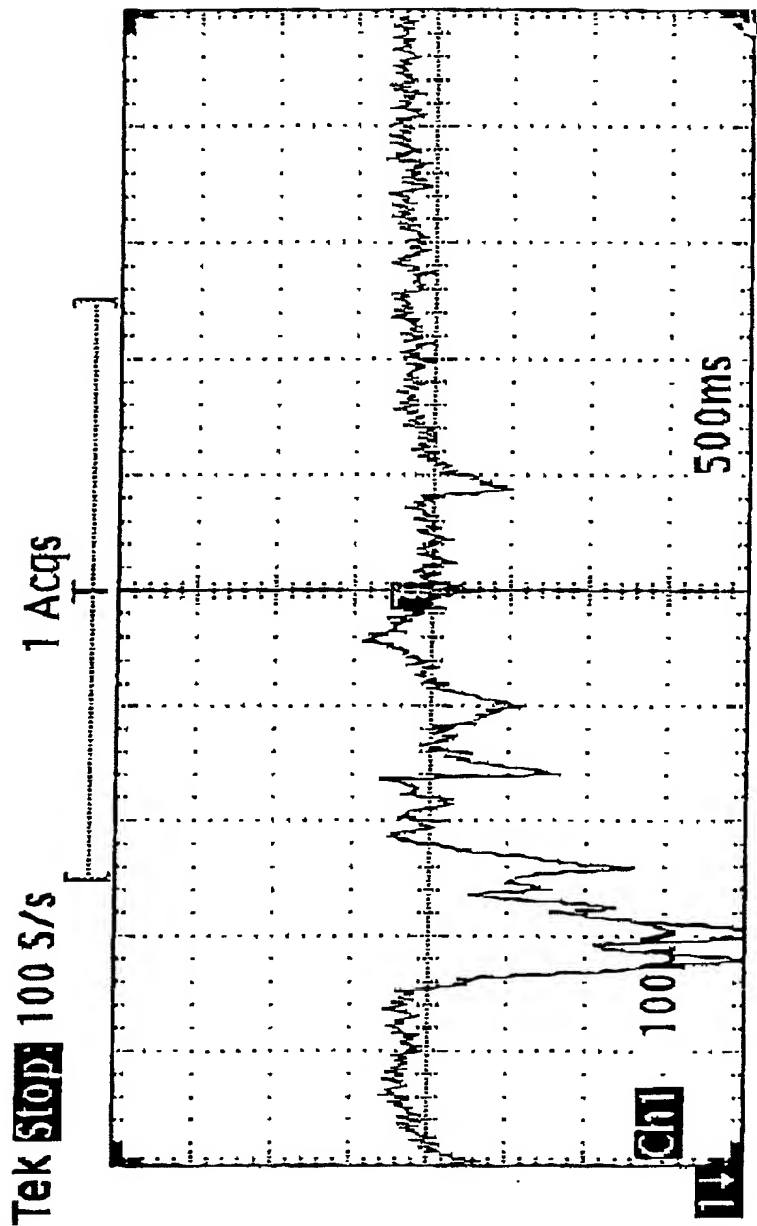
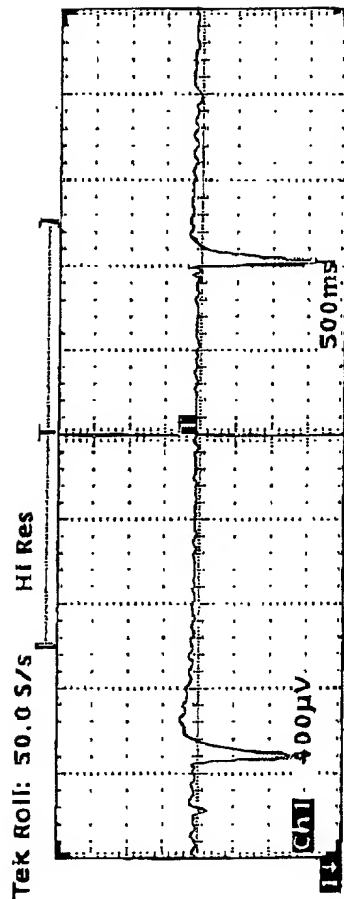
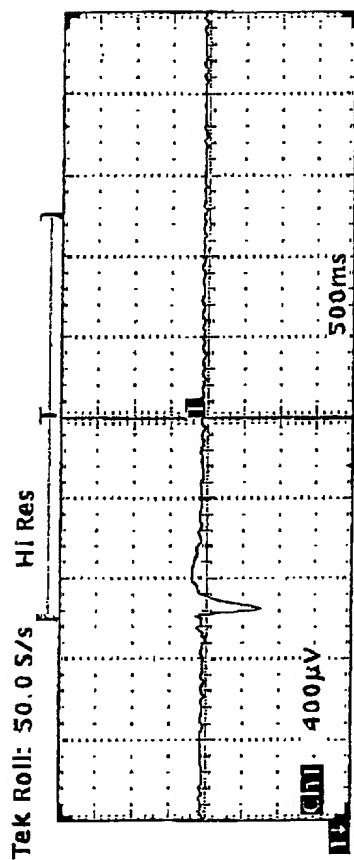


Figure 18 A: some sample charge sequencing extension signatures for 300 bp DNA



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Figure 18 B: More sample charge sequencing extension signatures for 300 bp DNA with two different concentration of immobilized DNA (0.05 pmol and 0.1 pmol)

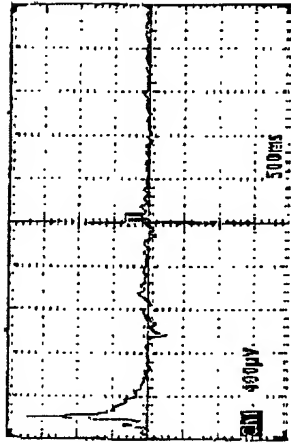


Figure 18C.

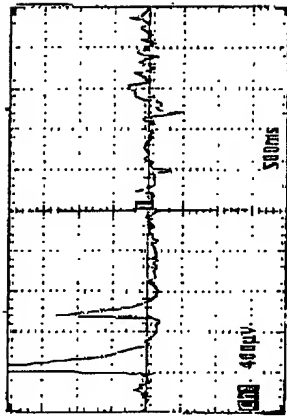


Figure 18D.

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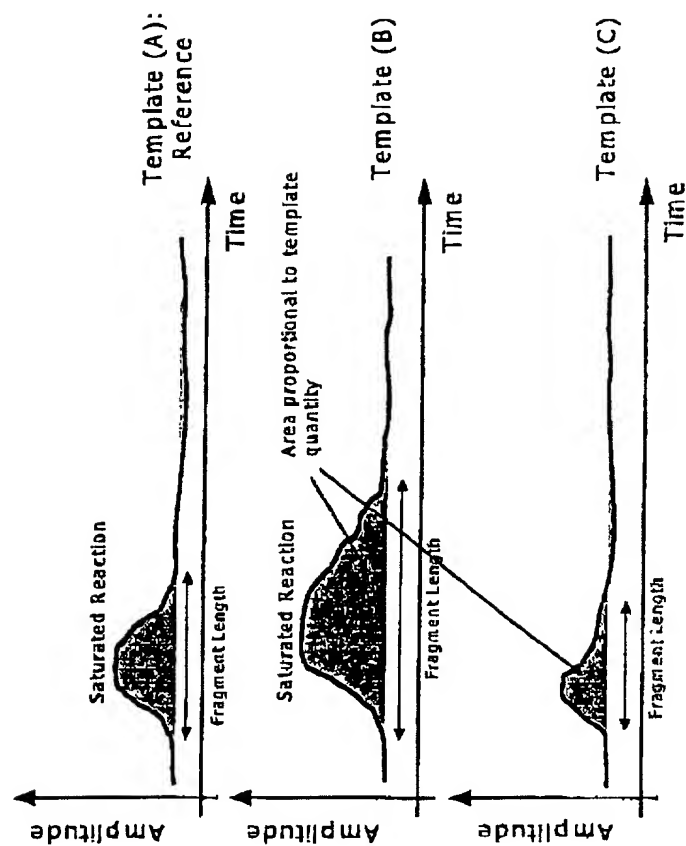
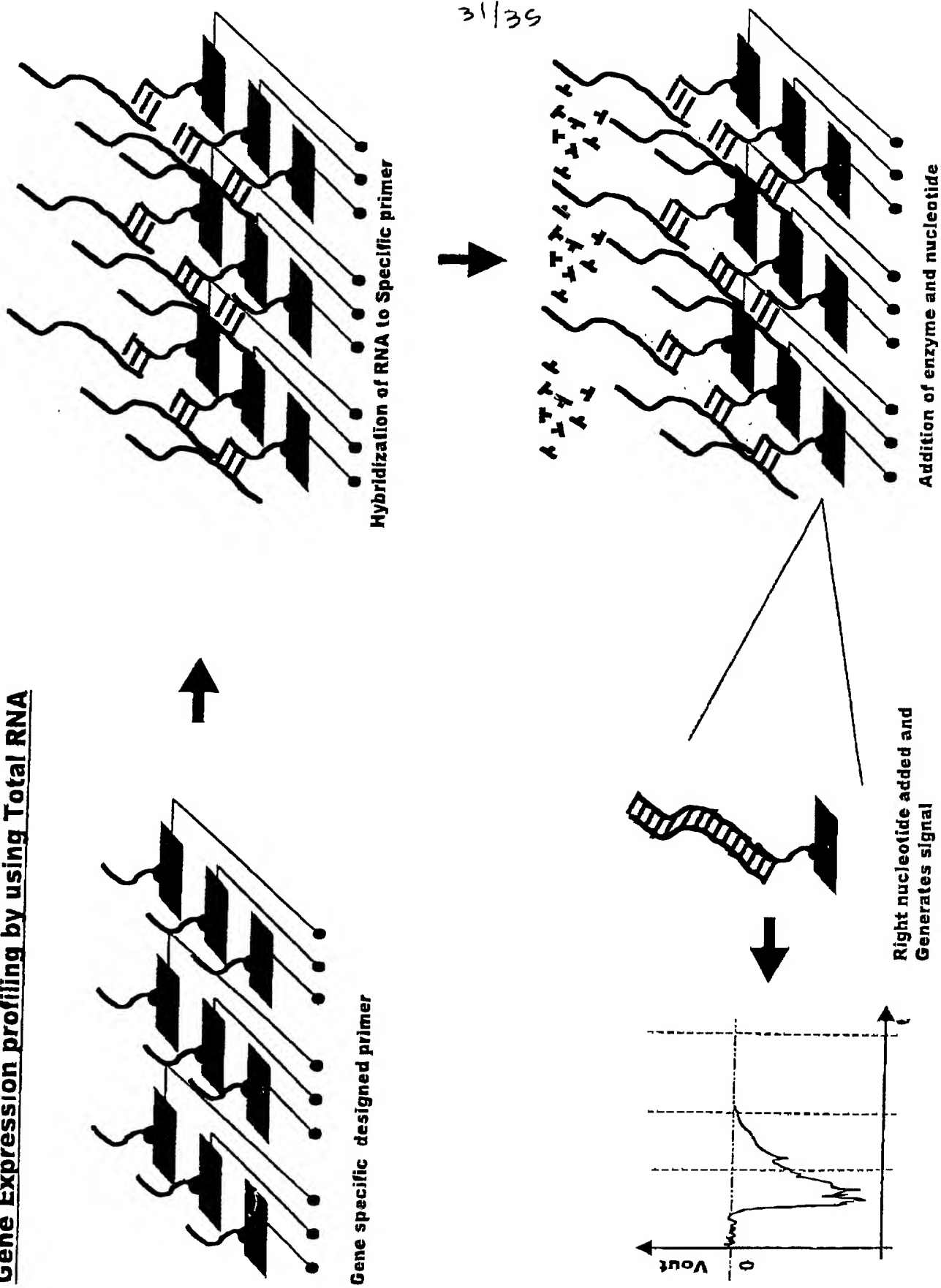


FIGURE 18E

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FIGURE 19 a:

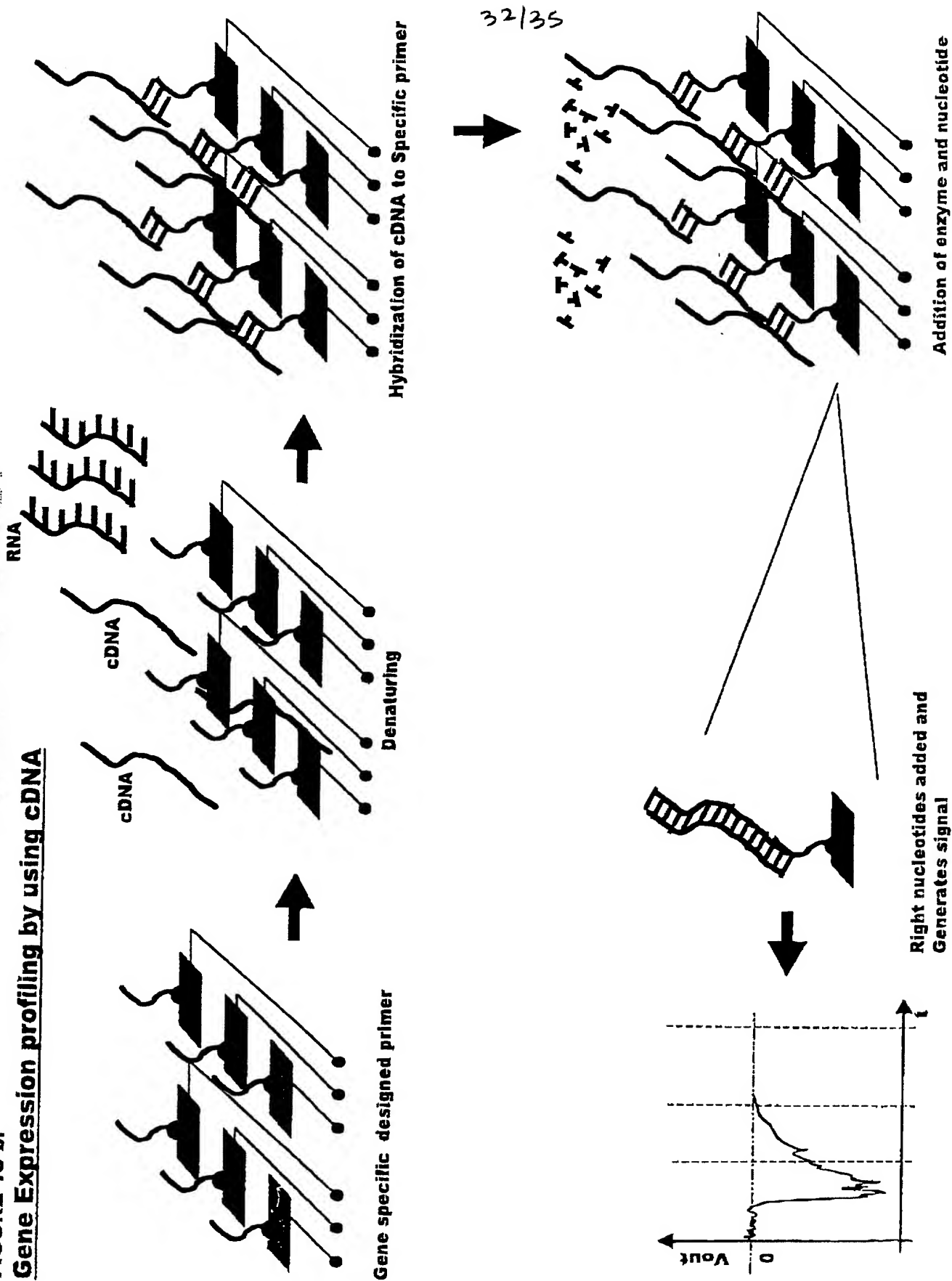
Gene Expression profiling by using Total RNA



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FIGURE 19 b:

Gene Expression profiling by using cDNA



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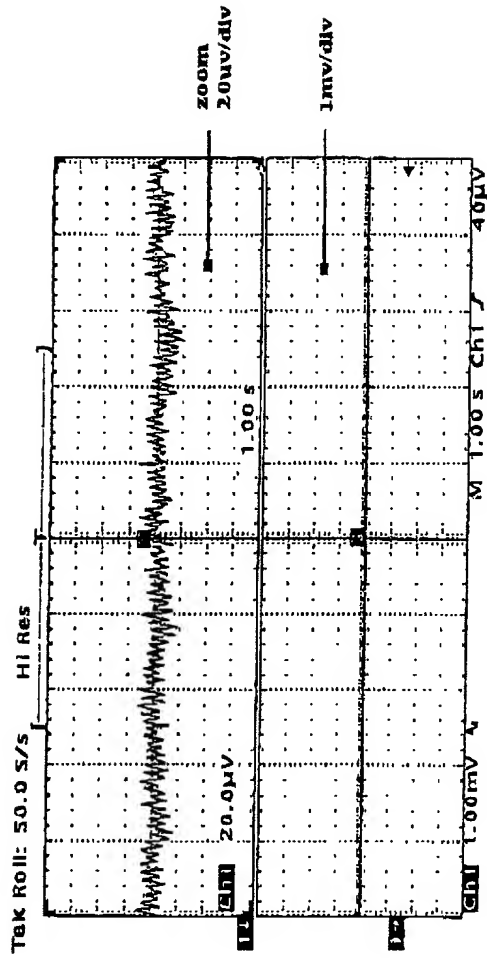


Figure 20

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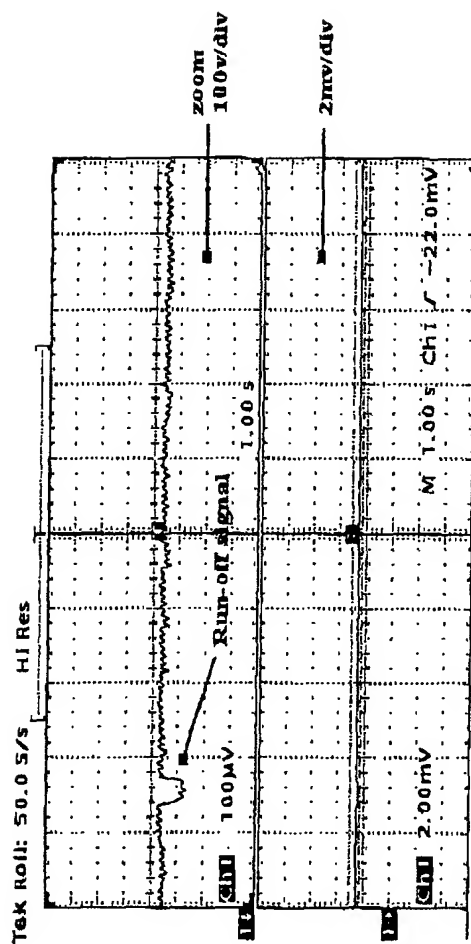


Figure 21

Figure 22

